Remarks

Applicants respectfully request and withdrawal of the rejections of the claims, in view of their remarks and amendment presented herein. Applicants have amended claims 1 and 31.

Claims 1-3, 14, 15, 19, and 28-31 are pending. No new matter has been added by amendment of the claims.

Applicants respectfully assert that the Examiner introduced a new ground of rejection that was not necessitated by amendment of claim 1, or addition of claims 30 and 31, and request withdrawal of the finality of the rejection.

35 U.S.C. § 112 Rejection of the Claims

The Examiner rejected claim 31 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Applicants have followed the Examiner's suggestions regarding "glutonate" and "tributyrin". Applicants submit that these amendments overcome this rejection and consequently request its withdrawal.

35 U.S.C. § 102 Rejection of the Claims

The Examiner rejected claims 1-3, 14, 15, 19 and 28-31 under 35 U.S.C. § 102(e) as being anticipated by Brodbeck et al. (U.S. Patent No. 6,331,311). Applicants respectfully traverse this rejection. Brodbeck does not teach one of skill how or why to select the combination of ingredients composing Applicants' claimed composition. Moreover, Brodbeck actually leads one of skill away from Applicants' claimed composition.

Applicants' claimed composition is a two-phase emulsion system of a controlled release formulation and a biologically active mixture that do not appreciably mix. The controlled release formulation includes an organic solvent and a polymer. The biologically active mixture includes a biologically active agent and an aqueous medium. With this system, the aqueous medium isolates the biologically active agent from the polymer and the solvent and avoids the mutual degradation of agent and polymer. In order to accomplish isolation and avoid appreciable mixing, Applicants' claimed composition contains an organic solvent having a water solubility of

from about 2 to about 20 percent by weight relative to the combination of water and solvent. Applicants have found that a higher water solubility results in an intractable, solid material as indicated in example 2 of the present application. Applicants have also found that a significantly lower water solubility does not enable facile formation of the emulsion.

In contrast to Applicants' claimed invention, Brodbeck does not disclose a controlled release formulation that contains only an organic solvent having a water solubility of from about 2 percent to about 20 percent by weight relative to a weight of a combination of organic solvent and water. Rather, Brodbeck discloses that gel depot compositions can include solvents having a wide variety of solubility characteristics, as indicated above. Solvents included in this list include those that are insoluble or practically insoluble in water, such as benzyl benzoate and oleic acid respectively, as well as solvents that are soluble in water, such as glycerol formal, methyl acetate, dimethyl sulfoxide, and caprolactam. (See Brodbeck, col. 5, lines 6-30.) Brodbeck also discloses that preferred solvents include triacetin (soluble in water and miscible with alcohol) and N-methyl-2-pyrrolidone (miscible with water and alcohol). Brodbeck does not disclose any criteria used to select an organic solvent based on solubility, but rather indicates that solvents having a wide range of solubility characteristics are acceptable for use in the gel depot compositions. Therefore, Brodbeck leads away from solvents having a water solubility of from about 2 percent to about 20 percent by weight relative to a weight of a combination of organic solvents and water by directing the skilled art worker to preferred solvents that are soluble or miscible with water.

As demonstrated by Applicants in Example 1 of the specification, use of water in polymer solutions prepared with low water-soluble solvents produces an emulsion that can be expressed from a syringe having a 20-gauge cannula into phosphate buffered solution to form an intact implant. However, as demonstrated by Applicants' comparative Example 2, use of water in polymer solutions prepared with highly-water soluble solvents, such as Brodbeck's preferred solvent N-methyl-2-pyrrolidone, causes immediate coagulation of the polymer solution to form a solid plug that cannot be expressed from a syringe. Thus, use of a solvent described by Brodbeck as being preferred in a composition claimed by the Applicants causes the composition to become inoperable as an injectable implant.

The Examiner has picked and chosen from among the many, many options and ingredients taught by Brodbeck and allegedly assembled Applicants' claimed composition. However, the Examiner has not explained how or why Brodbeck enables such picking and choosing. Nor has the Examiner pointed to any direction from Brodbeck for making such a selection. In particular, Applicants respectfully submit that Brodbeck does not anticipate the claims because Brodbeck does not teach how or why one might select a composition having an organic solvent with a water solubility of from about 2 percent to about 20 percent by weight relative to a weight of a combination of organic solvent and water. Applicants emphasize that Brodbeck directs one of skill away from Applicants' claimed composition because Brodbeck actually teaches the preferred use of solvents that cause Applicants' claimed composition to become inoperable. In fact, this Brodbeck teaching is Brodbeck's direction yet it leads one away from Applicants' claimed invention. Accordingly, Applicants respectfully request the Examiner to withdraw the rejection of the claims under 35 U.S.C. § 102(e).

Conclusion

Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney (612-373-6939) to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

RICHARD L. DUNN

By their Representatives,

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402
(612) 373-6939

Date Sept 30, 2002 By A. James Nelson

A. James Nelson
Reg. No. 28,650

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Box AF, Commissioner of Patents, Washington, D.C. 20231, on this 30th day of September, 2002.

Dawn M. Poole
Name

Dawn M. Poole
Signature

CLEAN VERSION OF PENDING CLAIMS

EMULSIONS FOR IN-SITU DELIVERY SYSTEM
Applicant: Richard L. Dunn
Serial No.: 09/060,047

1. (Amended) A composition for delivering a biologically active agent, comprising: an emulsion of a biologically active mixture and a controlled release formulation, the biologically active mixture comprising the biologically active agent and a pharmaceutically acceptable, aqueous medium as a protective carrier; and the controlled release formulation comprising a pharmaceutically acceptable, biodegradable thermoplastic polymer that is substantially insoluble in an aqueous or body fluid and a pharmaceutically acceptable organic solvent having a water solubility of from about 2 percent to about 20 percent by weight relative to a weight of a combination of organic solvent and water.

2. A precomposition suitable for preparing a composition according to claim 1, comprising separate containers of the biologically active mixture and controlled release formulation, which containers are adapted to cause combination of the biologically active mixture and controlled release formulation.

3. A composition of claim 1, wherein the biologically active agent is selected from the group consisting of an antiinflammatory agent, an antibacterial agent, an antifungal agent, an analgesic agent, an anesthetic agent, an immunogen, a vaccine, an antineoplastic agent, a growth or survival agent, a hormone, a cardiovascular agent, an anti-ulcer agent, a bronchial agent, a central nervous system agent, a gene, a gene fragment, an insertion vector carrying a gene or gene fragment, and any combination or multiple thereof.

14. (Amended) A composition of claim 1 wherein the thermoplastic polymer formula contains monomeric units selected from the group consisting of lactide, glycolide, caprolactone, anhydride, amide, urethane, esteramide, orthoester, dioxanone, acetal, ketal carbonate, phosphazene, hydroxybutyrate, hydroxyvalerate, alkylene oxalate, alkylene succinate, amino acid and any copolymer and terpolymer combination of these monomeric units in random order or in block order.

15. A composition of claim 14 wherein the monomeric units include lactide, glycolide, caprolactone, hydroxybutyrate, and any combination thereof.

19. A composition of claim 1, wherein the emulsion is a water-in-oil emulsion.

28. A composition of claim 1 wherein the thermoplastic polymer is in mixture with a non-polymeric material.

29. A composition of claim 1 wherein the aqueous carrier is water, saline, physiological buffer solution, cell-culture medium, aqueous nutrient medium, aqueous mineral medium, aqueous amino acid medium, aqueous lipid medium, aqueous vitamin medium or any combination thereof.

30. (Amended) A composition of claim 1 wherein the organic solvent is selected from the group consisting of propylene carbonate, diethyl malonate , ethylene carbonate, dimethyl carbonate, 2-ethoxy ethyl acetate, ethyl acetate, methyl acetate, ethyl butyrate, diethyl glutarate, tributyl citrate, diethyl succinate, isopropyl myristate, dimethyl adipate, dimethyl succinate, dimethyl oxalate, dimethyl citrate, triethyl citrate, acetyl tributyl citrate, glyceryl triacetate, methyl ethyl ketone, tetrahydrofuran,

31. A composition of claim 1 wherein the organic solvent is selected from the group consisting of propylene carbonate, diethyl malonate , ethylene carbonate, dimethyl carbonate, 2-ethoxy ethyl acetate, ethyl acetate, methyl acetate, ethyl butyrate, diethyl glutonate, tributyl citrate, diethyl succinate, tributyrin, isopropyl myristate, dimethyl adipate, dimethyl succinate, dimethyl oxalate, dimethyl citrate, triethyl citrate, acetyl tributyl citrate, glyceryl triacetate, methyl ethyl ketone, tetrahydrofuran,

CLEAN VERSION OF AMENDED SPECIFICATION PARAGRAPHS

EMULSIONS FOR IN-SITU DELIVERY SYSTEM
Applicant: Richard L. Dunn
Serial No.: 09/060,047

Please substitute the following paragraph for the paragraph starting on page 13, line 23 and ending on page 14, line 5 of the specification.

Examples of low water soluble solvents include ethyl acetate, propylene carbonate, diethyl malonate esters of carbonic acid and alkyl alcohols such as propylene carbonate, ethylene carbonate and dimethyl carbonate alkyl esters of mono-, di-, and tricarboxylic acids, such as 2-ethyoxyethyl acetate, ethyl acetate, methyl acetate, ethyl butyrate, diethyl malonate, diethyl glutarate, tributyl citrate, diethyl succinate, tributyrin, isopropyl myristate, dimethyl adipate, dimethyl succinate, dimethyl oxalate, dimethyl citrate, triethyl citrate, acetyl tributyl citrate, glyceryl triacetate; alkyl ketones such as methyl ethyl ketone, tetrahydrofuran as well as other carbonyl, ether, carboxylic ester, amide and hydroxy containing liquid organic compounds having some solubility in water. Propylene carbonate, ethyl acetate, triethyl citrate, isopropyl myristate, and glyceryl triacetate are preferred because of biocompatibility and pharmaceutical acceptance.